IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Daisuke SHOJI et al.	Group Art Unit : 1763	
Appl. No.	: 10/599,435	Examiner : Chun Cheng WANG	
Filed	: September 28, 2006	**Confirmation No. : 8794**	
For	: METHOD FOR CONTROLLING AVERAGE PORE DIAMETER OF POROUS BODY COMPRISING APATITE/COLLAGEN COMPOSITE FIBERS		

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Appeal Brief - Patents
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

This Appeal is from the Examiner's rejection of claims 1 and 3 set forth in the Final Office Action mailed from the U.S. Patent and Trademark Office on June 10, 2010.

A Notice of Appeal in response to the June 10, 2010 Final Office Action was filed on December 9, 2010.

The requisite fee under 37 C.F.R. § 41.20(b)(2) for filing this Appeal Brief is being paid concurrently herewith. The Patent and Trademark Office is hereby authorized to charge any additional fees that may be deemed necessary for maintaining the pendency of this application, including any appeal or extension of time fees that may be deemed necessary, to Deposit Account No. 19-0089.

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I. REAL PARTY IN INTEREST

The real parties in interest in this appeal are Pentax Corporation of Tokyo, Japan and National Institute for Materials Science of Ibaraki-ken, Japan. The corresponding assignment was recorded in the U.S. Patent and Trademark Office on December 12, 2006 at REEL 018618, FRAME 0255.

II. RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' representative or the Assignees are not aware of any prior and pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

The status of the claims is as follows:

Claims 1 and 3 are pending in this application.

Claims 2 and 4 are cancelled.

Each of claims 1 and 3 is indicated as rejected in the Final Office Action mailed June 10, 2010.

The rejection of each of claims 1 and 3 is under appeal. Claims 1 and 3 involved in the appeal are reproduced in the Claims Appendix attached hereto.

IV. STATUS OF AMENDMENTS

An Amendment was filed subsequent to the Final Office Action of June 10, 2010 on November 10, 2010. According to the Advisory Action mailed November 23, 2010 the Amendment and the Declaration under 37 C.F.R. § 1.132 submitted therewith have been entered and considered by the Examiner.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Claim 1

Independent claim 1 is drawn to a method for controlling the average pore diameter of a porous body comprising a fibrous apatite/collagen composite. The porous body is produced by gelating a dispersion comprising said fibrous apatite/collagen composite, collagen and water, freeze-drying the resultant gel to form a porous body, and cross-linking the collagen in said porous body. The average pore diameter of the porous body is controlled as follows and in the following order:

a) freezing a plurality of gels at various freezing-environment temperatures (T_0) and measuring the solidification time (Sb) of each gel to prepare a graph showing the relation between the freezing-environment temperature and the solidification time;

b) measuring the average pore diameter (D_{AV}) of the porous body obtained at various lengths of solidification time to prepare a graph showing the relation between solidification time and average pore diameter;

c) determining the solidification time for providing a desired average pore diameter of said porous body from the graph of the solidification time and the average pore diameter; and

d) determining the freezing-environment temperature for achieving the determined solidification time from the graph of the freezing-environment temperature and the solidification time.

See, e.g., page 3, lines 8-20, page 10, line 26 to page 11, line 2, page 11, line 27 to page 12, line 3 and page 13, lines 1-14 of the present specification.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The broad issue under consideration is:

Whether claims 1 and 3 are properly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kikuchi et al., Key Engineering Materials, 2004, Vols. 254-256, pp. 561-564 (hereinafter "KIKUCHI"), and in particular, whether the disclosure of KIKUCHI are sufficient to establish a *prima facie* case of obviousness of the subject matter of claims 1 and 3.

VII. ARGUMENTS

A. Citation of Authority

Obviousness

The appropriate starting point for a determination of obviousness is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 U.S.P.Q. 459, 466 (1966):

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

"A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). The relevant question is "whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *Id.*

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

B. Claims 1 and 3 Are Not Properly Rejected Under 35 U.S.C. 103(a) As Being Unpatentable Over KIKUCHI

1. Summary of Rejection

The rejection refers to paragraph 3 of the Office Action mailed November 2, 2009 wherein it is essentially alleged that KIKUCHI discloses the claimed method with the exception that KIKUCHI is silent on charting solidification time, Sb, vs. average pore diameter, D_{AV}, and freezing-environment temperature, T_0, vs. solidification time. In the latter respect the Examiner asserts that KIKUCHI discloses using the freezing temperature to control the pore size of the fibrous apatite/collagen composite and the relationship between solidification time vs. pore size, wherefore it would allegedly have been obvious to one of ordinary skill in the art to measure Sb (because for a system for which the completely solidified state cannot easily be monitored Sb allegedly is a convenient indicator for the completion of the solidification treatment) and to plot the charts of Sb vs. D_{AV} and T_0 vs. Sb (instead of plotting D_{AV} vs. T_0 directly). Further, in the

Advisory Action mailed November 23, 2010 the Examiner essentially dismisses the results set forth in the Declaration under 37 C.F.R. § 1.132 submitted on November 10, 2010) as allegedly unsuitable for evidencing a surprising and favorable effect (i.e., much higher accuracy in predicting the measured D_{AV} with the claimed method compared to using a graph of D_{AV} vs. T_0) due to the allegedly large error margins involved.

2. Traverse

a. KIKUCHI fails to provide an apparent reason for one of ordinary skill in the art to measure as Sb and to plot it vs. D_{AV} and vs. T_0

Appellants submit that according to the claimed method the expected average pore diameter, D_{AV}, in the porous body recited in instant claim 1 is not determined as a function of the freezing-environment temperature, T_0, at which a gel comprising a fibrous apatite/collagen composite, collagen and water is frozen but is determined by additionally using an "intermediate" parameter, e.g., the solidification time Sb, i.e., the time it takes for the gel to solidify at a given temperature T_0, and by plotting (i) Sb vs. D_{AV} and (ii) T_0 vs. Sb for a plurality of gels.

Even if one were to assume, *arguendo*, that KIKUCHI indicates that there is a relationship between average pore diameter and freezing-environment temperature, KIKUCHI clearly contains not more than an indirect reference to the solidification time. In particular, the only (very indirect) reference to a solidification time in KIKUCHI is in the last paragraph of page 562 thereof wherein it merely is mentioned that "[t]he rapid decreasing of temperature of the gelled mixture resulted in nucleation of large amounts of ice crystals and ice crystals between the fibers became smaller. Consequently, larger

amounts of smaller pore were formed in the porous body frozen in lower temperature in comparison to that prepared at higher freezing temperature."

Accordingly, KIKUCHI (merely) teaches that a lower freezing temperature will result in smaller pores. Since it is reasonable to assume that the solidification time decreases with decreasing freezing temperature one of ordinary skill in the art may conclude from KIKUCHI that the average pore size decreases with decreasing solidification time. It is pointed out however, that this relationship between solidification time and average pore size is not spelled out in KIKUCHI and that there clearly is no teaching or suggestion in KIKUCHI that one should pay attention to the solidification time <u>in addition</u> to the freezing temperature in this regard.

It further is noted that the <u>only</u> alleged reason stated by the Examiner as to why one of ordinary skill in the art would pay attention to (i.e., would measure) the solidification time is that "[f]or a system that the complete solidified state can not be easily monitored, <u>the Sb is a convenient indicator for the completion of solidifying treatment</u>". Office Action mailed November 2, 2010, page 3, third paragraph; underlining in original.

Appellants submit that the Examiner's quoted allegation is <u>conclusory</u>. In particular, it is not seen that in the system of KIKUCHI the completely solidified state "can not be easily monitored" and it also is not seen why the solidification time is "a convenient indicator for the completion of solidifying treatment", and neither does the Examiner provide any explanation in this regard. At any rate, if it is difficult to monitor the completion of the solidifying treatment, as alleged by the Examiner, it should also be

difficult to determine the (exact) point of time at which the solidifying treatment is complete and thus, the (exact) solidification time.

To sum up, KIKUCHI is devoid of any teaching or suggestion to the effect that one should pay attention to the solidification time of the frozen gel, let alone to plot the solidification time vs. both the freezing-environment temperature and the average pore diameter (instead of directly plotting freezing-environment temperature vs. average pore diameter) in order to be able to predict the average pore diameter resulting from a given freezing-environment temperature (or to determine the freezing-environment temperature required for attaining a desired average pore diameter) with a high degree of accuracy. For this reason alone, KIKUCHI is unable to render obvious the subject matter of the instant claims.

b. The claimed method affords an unexpected favorable effect

As can be taken from the Declaration under 37 C.F.R. § 1.132 submitted on November 10, 2010 (hereafter "the Declaration"), the present method and in particular, measuring the average pore diameter (D_{AV}) of a porous body obtained at various lengths of solidification time and preparing a graph of solidification time vs. average pore diameter, determining the solidification time for providing a desired average pore diameter of said porous body from this graph, and determining the freezing-environment temperature for achieving the determined solidification time from a graph of the freezing-environment temperature vs. the solidification time, results in a much more accurate determination (prediction) of the freezing-environment temperature that is needed to achieve a desired average pore diameter than a method wherein the average pore

diameter is plotted vs. the freezing-environment temperature and the required freezing-environment temperature is directly determined from the resultant graph.

Specifically, from Fig. 6A and Fig. 8A of the Declaration (illustrating the method of the present invention for a specific porous body) it can be taken that a freezing-environment temperature T_0 of – 60 °C corresponds to a solidification time Sb of 1102 seconds (Fig. 6B), which in turn corresponds to an average pore diameter D_{AV} of <u>206 µm</u>.

In comparison, as can be taken from Fig. 9A of the Declaration, taking a "shortcut" by eliminating the solidification time as a parameter to be determined and determining D_{AV} directly from a graph of D_{AV} vs. T_0 would lead one to conclude that a freezing-environment temperature of – 60 °C results in an average pore diameter of <u>216 µm.</u>

The <u>experimentally determined</u> average pore diameter is <u>205.3 µm</u>, i.e., almost identical to the average pore diameter predicted on the basis of the method of the present invention but <u>more than 10 µm lower</u> than the value predicted on the basis of the "shortcut" method.

In other words, the (indirect) method of the present invention affords a much <u>more accurate prediction</u> of the average pore size that results from a given freezing-environment temperature than a direct method that dispenses with the measurement of the solidification time, contrary to what one of ordinary skill in the art would expect.

Appellants note that in response to the just described unexpected results the Examiner alleges in the last paragraph of the Continuation Sheet of the Advisory Action mailed November 23, 2010:

> The difference between the calculated pore diameter and measured pore diemerter [*sic*] is 0.7 µm for the instant application and is 10.7 µm for the Kikuch method

> [*sic*]. Applicant also indicated the pore diameter standard deviations (STD) for different average pore diameter (Avg) as 97±71 μm, 330±150 μm and 619±411 μm (Avg±STD; See TABLE 3 of the instant Specification). The difference between the calculated pore diameter according to the instant method and the Kikuch method [*sic*] is not significant or more accurate when compared with measurement of the pore diameter standard deviations that are greater than 71 μm.

The above allegations appear to indicate that the Examiner is of the opinion that an average pore diameter of, e.g., 97±71 μm means that the average pore diameter is somewhere between 26 μm (97-71) and 168 μm (97+71).

Appellants submit that the Examiner's (presumed) understanding of the meaning of the standard deviation (STD) of an average value based on the obtained set of measured values whose average is to be calculated is clearly incorrect. The STD does not indicate the margin of error of the average value, but rather is an indication of the extent to which all of the measured values are scattered around the average value that is calculated from these measured values.

In other words, the STD does not indicate any uncertainty with respect to the average value associated therewith but merely indicates how far the measured values which were used for calculating the average value as a whole are from the calculated average value thereof. This is illustrated by a simple example taken from http://en.wikipedia.org/wiki/Standard_deviation (which provides a good explanation of STD):

> A slightly more complicated real life example, the average height for adult men in the United States is about 70 inches (178 cm), with a standard deviation of around 3 inches (8 cm). This means that most men (about 68%, assuming a normal distribution) have a height within 3 in (8 cm) of the mean (67–73 in/170–185 cm), one standard deviation, and almost all men (about 95%) have a height within 6 in (15 cm) of the mean (64–76 in/163–193 cm), 2 standard deviations. If the standard deviation were zero, then all men would be exactly 70 in (178 cm) high. If the standard deviation were 20 in (51 cm), then men would have much more variable

> heights, with a typical range of about 50–90 in (127–229 cm). Three standard deviations account for 99.7% of the sample population being studied, assuming the distribution is normal (bell-shaped).

Applying the Examiner's (presumed) understanding of the meaning of STD to the above example the average height of adult men in the United States would not be 70 inches but could be as low as 67 inches and as high as 73 inches (for a STD of 3 inches). On the contrary, the average height of adult men in the United States invariably is (exactly) 70 inches, regardless of whether the STD is 3 inches or 20 inches.

In view of the foregoing explanation it should be apparent that there is no point in comparing the difference in the predicted average pore size according to the instant invention and according to the "shortcut" method with the standard deviation indicated for a specific average pore size. In particular, the difference in the predicted average pore size is a "real" value whereas the STD is only a measure of the distribution (scattering) of a plurality of experimentally determined pore sizes around their (calculated) average.

VIII. CONCLUSION

Appellants respectfully submit that for at least all of the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness of the subject matter of claims 1 and 3 over KIKUCHI. The Board is, therefore, respectfully requested to reverse the Final Rejection, and to allow the application to issue in its present form.

Respectfully Submitted,
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CLAIMS APPENDIX

1. A method for controlling an average pore diameter of a porous body comprising a fibrous apatite/collagen composite, said porous body being produced by:

gelating a dispersion comprising said fibrous apatite/collagen composite, collagen and water;

freeze-drying the resultant gel to form a porous body; and

cross-linking the collagen in said porous body,

wherein the average pore diameter of the porous body is controlled by the following in the following order:

a) freezing pluralities of gels at various freezing-environment temperatures and measuring the solidification time of each gel to prepare a graph showing the relation between the freezing-environment temperature and the solidification time;

b) measuring the average pore diameter of the porous body obtained at various lengths of solidification time to prepare a graph showing the relation between solidification time and average pore diameter;

c) determining the solidification time for providing a desired average pore diameter of said porous body from the graph of the solidification time and the average pore diameter; and

d) determining the freezing-environment temperature for achieving the determined solidification time from the graph of the freezing-environment temperature and the solidification time.

3. The method for controlling the average pore diameter according to claim 1, wherein the temperature for keeping said gel for freezing is -100°C to 0°C.

EVIDENCE APPENDIX

Declaration under 37 C.F.R. § 1.132 by Daisuki Shoji, submitted with Amendment filed November 10, 2010 (entered and considered by the Examiner; see Advisory Action mailed November 23, 2010).

RELATED PROCEEDINGS APPENDIX

None.